Management of Periocular Granuloma Annulare Using Topical Dapsone

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ABSTRACT

Granuloma annulare is a disease characterized by granulomatous inflammation of the dermis. Localized granuloma annulare may resolve spontaneously, while generalized granuloma annulare may persist for decades. The authors present the case of a 41-year-old Hispanic man with a two-week history of periocular granuloma annulare. Due to previously reported success in the use of systemic dapsone for the treatment of granuloma annulare, and the periocular proximity of the patient's lesion, topical dapsone was used for treatment. Various additional therapies for the management of granuloma annulare have been reported, such as topical and systemic steroids, isotretinoin, pentoxifylline, cyclosporine, Interferon gamma, potassium iodide, nicotinamide, niacinamide, salicylic acid, fumaric acid ester, etanercept, infliximab, and hydroxychloroquine. Additional clinical trials are necessary to further evaluate the effectiveness of topical dapsone in the management of granuloma annulare. (*J Clin Aesthet Dermatol.* 2015;8(7):48–51.)

Granuloma annulare (GA) was first identified in 1985 by Fox[1] and has since been well-described in the literature as benign, firm, skin-colored, and solitary or grouped papules or nodules arranged in an annular pattern.[2] When the nodules increase in size the annular ring arrangement can become obscured.[3] GA most commonly occurs in women in the first three decades of life.[2] The estimated distribution of GA lesions per the literature is 60 percent on the hands or arms, 20 percent on the feet and legs, seven percent involving both upper and lower extremities, five percent on the trunk, and five percent involving any other areas, such as the face and scalp.[4] It is rare to see GA on the face and scalp especially in adults as it usually occurs in children.[3] There have however been some instances of GA occurring on the face in adults as reported by Coskey in 1979 who studied the literature and found 44 reported cases of facial GA of which 25 were adults.[5] There are four subtypes of GA: localized, perforating, subcutaneous, and generalized.[3] The most common subtype is localized GA, which occurs in children and presents clinically as small, firm, asymptomatic, skin-colored or red papules or nodules in an arciform pattern and is histologically consistent with no epidermal change. This type runs the course of enlargement and later regression.[3] The second type is the perforating type, which appears as umbilicated lesions. The third type is subcutaneous GA, which appears clinically as subcutaneous nodules either mobile or fixed to the periosteum or bone located most commonly on the extremities.[3] The fourth type is generalized/disseminated GA, which occurs primarily in adults and presents as widespread flesh-colored to violaceous papules or plaques. Although there is some controversy over this relationship, generalized GA has been accepted to be significantly associated with diabetes mellitus.[3]

CASE REPORT

A 41-year-old Hispanic man presented to the authors' clinic with a two-week history of a newly formed facial lesion. He stated the lesion had a rapid onset, but denied any associated symptoms, including tenderness or pruritis. He denied previously having any similar cutaneous findings. The patient was in otherwise good health with no other pertinent medical history.

On physical exam, a 7mm erythematous granulomatous arcuate plaque was appreciated on the right lateral canthus, and a 4mm erythematous granulomatous papule on the upper right cutaneous eyelid (Figures 1 and 2). These clinical findings were suspicious for a granulomatous dermatoses, including sarcoidosis, granuloma annulare, or

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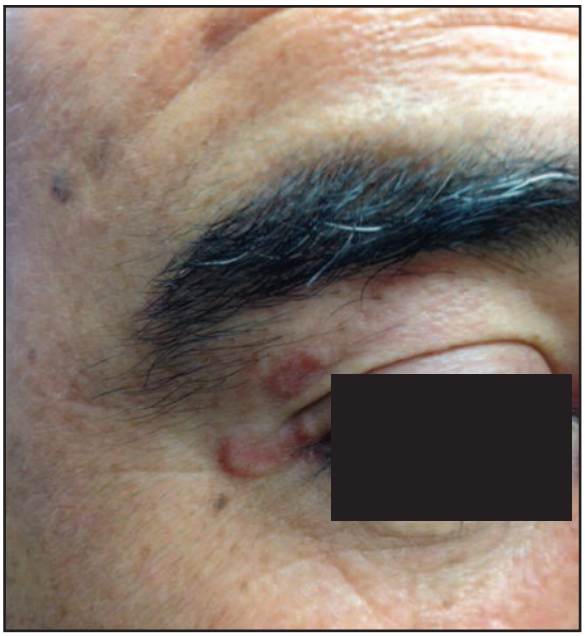
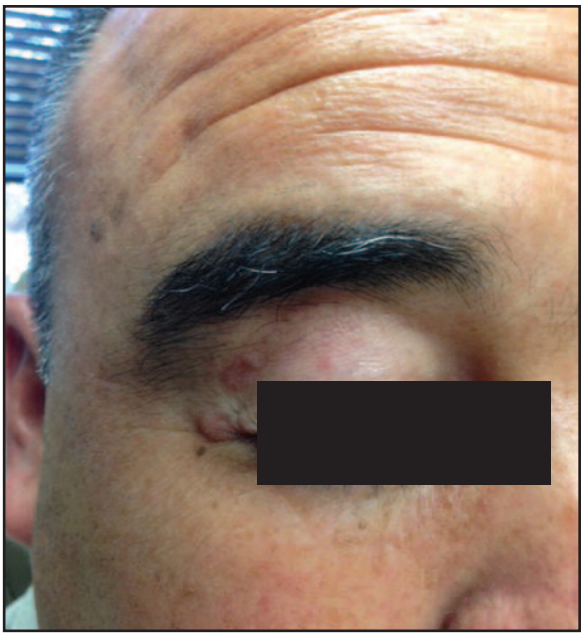



Figures 1 and 2. A 41-year-old Hispanic man presented with a 7mm erythematous granulomatous arcuate plaque on the right lateral canthus, and a 4mm erythematous granulomatous papule on the upper right cutaneous eyelid

malignancy. A punch biopsy was performed on the right lateral canthus. The histopathologic findings demonstrated interstitial collection of histiocytes surrounding areas of mucinous degeneration of collagen, with associated chronic inflammatory cells, rare giant cells, and absence of any cytologic atypia (Figures 3 and 4). Therefore, a diagnosis of granuloma annulare was made.

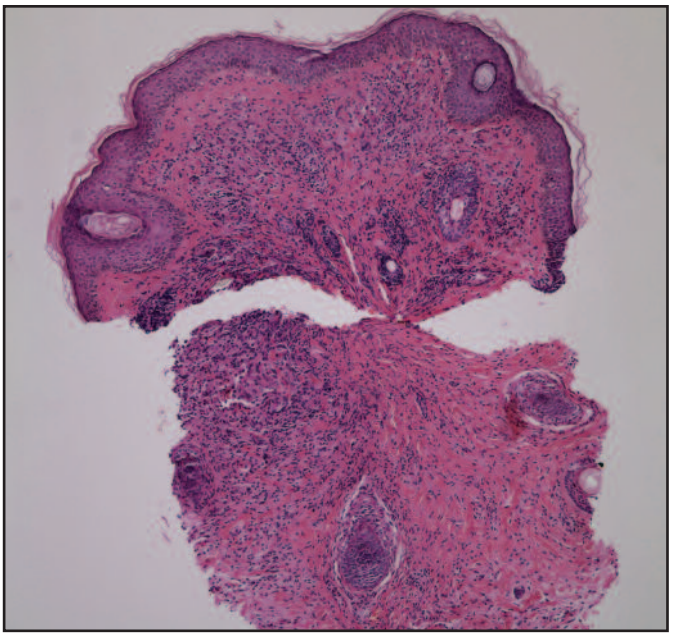
Various treatments have been reported in the management of granuloma annulare. Due to the patient's skin type of Fitzpatrick IV, and the proximity of the lesion to his eye, the authors opted to treat him topically without the risk of atrophy and hypopigmentation that exists with topical or intralesional topical corticosteroids. Systemic dapsone has been shown effective in the treatment of granuloma annulare, but to the authors' knowledge, has never been used in the topical treatment of granuloma annulare. The patient was started on a course of topical dapsone 5% gel (Aczone®, Allergan, Inc., Irvine California), which was applied twice daily to the lesion. After three weeks, the patient demonstrated significant clinical improvement (Figures 5 and 6). The authors believe the topical use of dapsone may have benefit in the management of granuloma annulare, specifically localized variants in cosmetically sensitive areas.

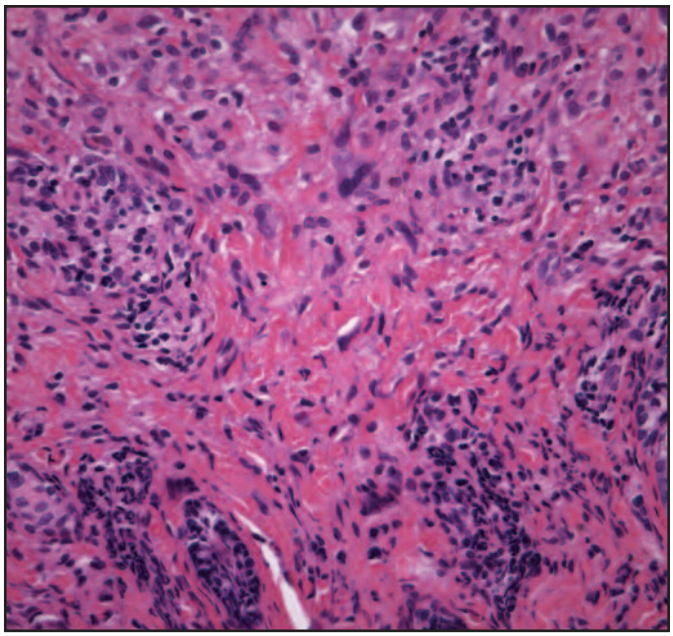
DISCUSSION

Granuloma annulare is a common inflammatory condition presenting with multiple skin-colored papules or nodules usually occurring in females before the age of 30. It is frequently located on the dorsal hands and feet, pretibial region, and the trunk.[3] Although deep, subcutaneous GAs have been reported in the periocular tissues, episclera, and orbit in children and young adults, a superficial dermal GA of the eyelid in an elderly patient is distinctly rare.

At the University of Michigan, Mesara et al[6] studied deep periocular nodular lesions and in 1964 named them pseudorheumatoid nodules in the opthalmologic pathology literature as they appeared pathologically identical to rheumatoid nodules. At the same time, these nodules were called granuloma annulare in the dermatological literature. Later in 1994, Burnstine et al[8] published a paper on the two oldest patients with periocular nodular lesions at age 60 and 62 and proceeded to call this granuloma annulare nodular type, which subsequently became the universal name for these lesions.[7]

The etiology of GA remains unclear; however, there are many known possible triggers, such as cutaneous infections, insect bites, sunlight exposure, and local trauma, which appear to be the most common reported association with GA in children with the subcutaneous type.[2] Granuloma annulare has also been seen at sites of healing herpes zoster and verruca vulgaris lesions, lending the suggestion of a viral etiology.[8] In addition, in 1977, Dahl et al[9] found immunoglobulin M (IgM) in the wall of blood vessels of the involved skin in 6 of 20 patients with GA, and found C3 in the blood vessel wall in 10 of 20 patients. Therefore, an immunoglobulin-mediated vasculitis has also been suggested as one possible etiology in GA. Furthermore, in 1976, Umbert and Winkelmann[10] found deposition of fibrin and circulating macrophage migration inhibition factors also known as lymphokines in the granulomas and necrobiotic lesions of 11 cases of GA, indicating an etiology of delayed hypersensitivity with involvement of the clotting factors.[10] The similarity of GA with sarcoidosis was also made evident by Umbert and Winkelmann who found that sarcoidosis and GA existed together in many cases, further adding to the





Figures 3 and 4. The histopathologic findings demonstrated interstitial collection of histiocytes surrounding areas of mucinous degeneration of collagen, with associated chronic inflammatory cells, rare giant cells, and absence of any cytologic atypia

evidence that delayed hypersensitivity reactions are responsible for the formation of GA.[10]

The differential diagnosis of GA includes sarcoidosis, lupus miliaris disseminatus faciei, childhood granulomatous periorificial dermatitis, syringoma, papular mucinosis, basal cell carcinoma, molluscum contagiosum, Miescher's granuloma of the face, and atypical necrobiosis lipoidica.[2] GA located on the trunk is often misdiagnosed as tinea corporis, and GA of the ocular region is commonly misdiagnosed as molluscum contagiosum, basal cell carcinoma, pilomatricoma, neurofibroma, and syringoma due to the fact that it may not demonstrate its characteristic annular pattern. In children, periocular GA is often misdiagnosed as an epidermal inclusion cyst.[2]

However, GA must be mainly differentiated from sarcoidosis, as they may both have similar clinical and histopathologic findings. Sarcoidosis can occasionally be histologically differentiated by the lack of inflammatory cell infiltrate.[2] In 2013, Kang et al[11] reported the case of a 51-year-old woman with an orbital mass. An excisional biopsy was performed that was histologically identical to the diagnosis of GA. The pathologic findings demonstrated ill-defined granulomas with central necrosis, chronic inflammation, and degenerated collagen, consistent with the findings in GA; however, after a thorough systemic workup, the patient was diagnosed with systemic sarcoidosis.[11]

HISTOLOGY

Histologically, GA is characterized by palisading histiocytes and lymphocytes around well-defined centers of necrobiosis of degenerated collagen, fibrin, and excess mucin between areas of normal dermis. Mucin stained with colloidal iron or alcian blue is diagnostic of subcutaneous GA with the presence of eosinophils in the center of necrotic tissue. Around the necrobiotic areas, there are lobules of epithelioid cells and multinucleated giant cells.[3,5]

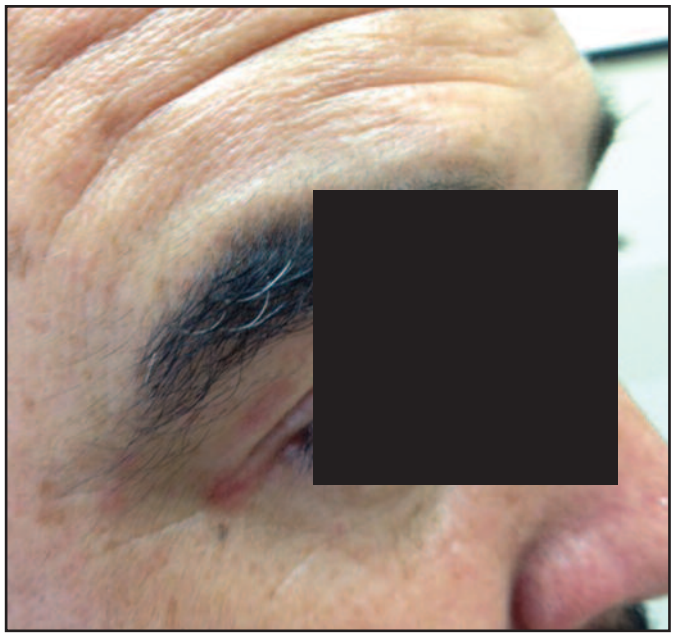
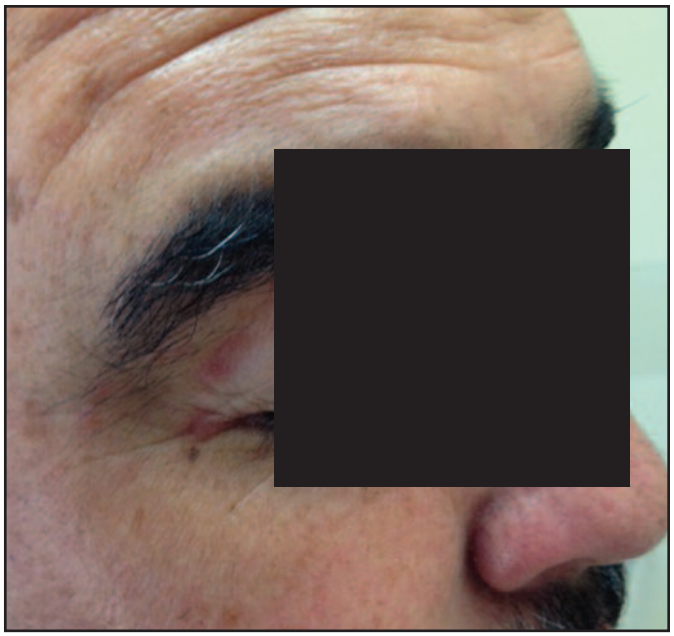
TREATMENT

There are many treatments for GA; however, treatment is often not necessary as these lesions tend to disappear within months to decades. Treatment includes both local and systemic forms of management. Local treatments include cryotherapy, excision, radiation therapy, laser treatment, and electrocoagulation. Systemic treatments include antimalarials, thyroxine, potassium iodide, and dapsone. Dapsone is a sulfone antibiotic that exhibits anti-inflammatory effects and has been successfully used in the management of disseminated GA.[12] Typically, systemic dapsone 100mg/day is recommended for disseminated GA, usually demonstrating improvement between 4 and 12 weeks after treatment.[13] Excision of lesions tends to be useful as a diagnostic approach more than a treatment, as these lesions often reoccur after removal. The most common treatments include topical and intralesional steroids.[3]

Treatment specific for periocular GA is controversial as many patients who have not undergone excision of their lesions tend to see spontaneous resolution within six months.[2]

CONCLUSION

Most cases of nodular GA are seen in children, as it is very rare to find periocular GA in an adult woman over the age of 30. The patient described herein represents the unique case of a 41-year-old man with a histologically defined diagnosis of periocular GA. The authors therefore emphasize the importance of having the diagnosis of GA in the differential

Figures 5 and 6. After a three-week course of topical dapsone 5% gel, which was applied twice daily to the lesion, the patient demonstrated significant clinical improvement

when treating older individuals who present with ocular and adnexal nodules, as they do not solely occur in children and young adults. In addition, as sarcoidosis and GA present very similarly clinically and histologically, the authors stress the importance of a complete systemic workup with the detection of an orbital granuloma to ensure accurate diagnosis and appropriate management.

Systemic dapsone has been previously reported in the treatment of GA. To the authors' knowledge, there are no reported cases of the use of topical dapsone in the treatment of localized GA. Due to the periocular location of the patient's lesion, the authors were able to treat him with topical dapsone 5% gel in a safe and effective way. Topical dapsone may be a consideration for the management of GA in areas localized to cosmetically sensitive areas where other treatment options may leave the patient at greater risk for pain, infection, and scarring.

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